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EXAMINER
CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,144	CHANG ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22,23,25-29 and 32-61* is/are pending in the application.

4a) Of the above claim(s) *19,20,22,23,25-29,33,35 and 37-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,32,34,36 and 45-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-22-04 & 2-15-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I, claims 1-18, 32-36 and 45-61, and species election of protein, peptide or hormone, in the reply filed on 3-15-07 is acknowledged. The traversal is on the ground(s) that there is no serious burden to search groups I-III, and not all proteins are enzymes and search for protein/peptides/hormones and antibodies/antibody fragments together would not place serious burden on the examiner. This is not found persuasive because of the reasons of record. Groups I-III are drawn to methods that have different design and different mode of operation. They are drawn to methods that differ at least in objectives, method steps, reagents and doses used, schedules used, response variables, and criteria of success. They have different classifications and there is serious burden for Examiner to search all of groups I-III. Proteins and antibodies are structurally distinct molecules; any relationship between a protein and an antibody is dependent upon the correlation between the scope of the proteins that the antibody binds and the scope of the antibodies that would be generated upon immunization with the protein. Therefore, a search for protein, peptide, or hormone does not require a search for antibody or antibody fragment, and vice versa. Thus, there would be serious burden for Examiner to search both protein/peptides/hormones and antibodies/antibody fragments together.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 19, 20, 22, 23, 25-29 and 37-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3-15-07.

Claims 1-20, 22, 23, 25-29 and 32-61 are pending. Claims 33 and 35 are drawn to antibody fragment. Therefore, claims 33 and 35 will NOT be considered at the present time. Claims 1-18, 32, 34, 36 and 45-61 and the elected species proteins, peptides, or hormones are under consideration.

Double Patenting

3. Applicant is advised that should claim 1 be found allowable, claim 46 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The vectors of claims 1 and 46 are drawn to a vector comprising a cell-targeting ligand non-covalently bound to a virus. The intended use of the vector does not carry weight in the component of the claimed vector. The following warnings are based on the same reason.

4. Applicant is advised that should claim 2 be found allowable, claim 47 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

5. Applicant is advised that should claim 3 be found allowable, claim 48 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight

difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

6. Applicant is advised that should claim 4 be found allowable, claim 49 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. Applicant is advised that should claim 5 be found allowable, claim 50 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

8. Applicant is advised that should claim 6 be found allowable, claim 51 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

9. Applicant is advised that should claim 7 be found allowable, claim 52 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

10. Applicant is advised that should claim 8 be found allowable, claim 53 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

11. Applicant is advised that should claim 9 be found allowable, claim 54 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

12. Applicant is advised that should claim 10 be found allowable, claim 55 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

13. Applicant is advised that should claim 11 be found allowable, claim 56 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

14. Applicant is advised that should claim 12 be found allowable, claim 57 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an

application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

15. Applicant is advised that should claim 13 be found allowable, claim 58 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

16. Applicant is advised that should claim 14 be found allowable, claim 59 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

17. Applicant is advised that should claim 15 be found allowable, claim 60 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

18. Applicant is advised that should claim 16 be found allowable, claim 61 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing,

despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 11, 32 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "EGF", "VEGF", "FGF" and "IGF" in claims 11 and 56 are vague and render the claims indefinite. Those terms are abbreviations that can stand for different meanings. It is unclear what meaning is intended in the claims for each term. Spelling out the terms would be remedial.

The term "EGF" in claim 32 is vague and renders the claim indefinite. The term "EGF" is an abbreviation that can stand for different meanings. It is unclear what meaning is intended in the claim. Spelling out the term would be remedial.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 1-6, 8-11, 17, 18, 32, 34, 45-51, 53-56 are rejected under 35 U.S.C. 102(a) as being anticipated by Sosnowski et al., 1998 (WO 98/40508, IDS).

The claims are directed to a vector for delivery of a virus, such as a retrovirus or an adenovirus, to a target cell within a host animal, comprising a cell targeting ligand, such as a protein, a peptide or a hormone, non-covelently bound directly to said virus, wherein said virus and said ligand are not naturally associated with each other, or said virus comprises a therapeutic nucleic acid encoding a therapeutic protein, such as wild-type p53, a method of preparing said vector, and a vector produced by said method. Claims 8 and 53 specify the virus is a chimeric virus, a hybrid virus or a recombinant virus. Claims 10 and 55 specify the cell-targeting ligand is a native protein or a recombinant protein. Claims 11 and 56 specify the cell-targeting ligand is selected from the group consisting of EGF, VEGF, FGF, IGF, a viral protein and a bacterial protein etc.

Sosnowski teaches preparation of a tropism-modified adenoviral vector specifically binds to target cells expressing a preselected receptor, comprising an antibody or fragment thereof that binds an adenoviral capsid protein, a targeting ligand that binds the preselected receptor, such as a polypeptide reactive with an FGF receptor, and an adenovirus containing a nucleic acid molecule encoding a therapeutic gene product under the control of a promoter, wherein the ligand is conjugated to the antibody or fragment thereof and wherein the antibody or fragment thereof is bound to the adenovirus (e.g. p. 171). The polypeptide reactive with an FGF receptor could be KGF, FGF-1 to FGF-15. The targeting ligand could be a polypeptide reactive with VEGF receptor, PDGF receptor or EGF receptor (e.g. p. 6, 172). Sosnowski also teaches that the

therapeutic gene product could be p53, IGF, TGF etc. (e.g. p. 7, second paragraph). Since the ligand is conjugated to the antibody or fragment thereof and the antibody or fragment thereof is bound to the adenovirus, therefore, the ligand is non-covelently bound to the adenovirus. Thus, claims 1-6, 8-11, 17, 18, 32, 45-51, 53-56 are anticipated by Sosnowski.

23. Claims 1-4, 6, 8-11, 17, 18, 45-49, 51 and 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Satyamoorthy et al., 1997 (Cancer Research, Vol. 57, p. 1873-1876).

The claims are directed to a vector for delivery of a virus, such as a retrovirus or an adenovirus, to a target cell within a host animal, comprising a cell targeting ligand, such as a protein, a peptide or a hormone, non-covelently bound directly to said virus, wherein said virus and said ligand are not naturally associated with each other, or said virus comprises a therapeutic nucleic acid encoding a therapeutic protein, a method of preparing said vector, and a vector produced by said method. Claims 8 and 53 specify the virus is a chimeric virus, a hybrid virus or a recombinant virus. Claims 10 and 55 specify the cell-targeting ligand is a native protein or a recombinant protein. Claims 11 and 56 specify the cell-targeting ligand is selected from the group consisting of EGF, VEGF, FGF, IGF, a viral protein and a bacterial protein etc.

Satyamoorthy teaches mixing a recombinant bFGF-SAP (basic fibroblast growth factor-plant toxin saporin) with a replication-defective adenovirus Ad5 containing LacZ reporter gene and shows that infection of melanoma cells with a replication-defective adenovirus enhances cell killing by a mitotoxin bFGF-SAP more than 10 fold (e.g. abstract, right column under Materials and Methods). Adenovirus infection leads to increased apoptosis by the mitotoxin due to enhanced internalization of the ligand-receptor complex and release of the active toxin from the

endosomes (e.g. abstract). LacZ gene is considered a therapeutic nucleic acid. A replication-defective adenovirus is considered a recombinant virus. The bFGF-SAP is a recombinant proptein and bFGF is considered a cell-targeting ligand. Thus, claims 1-4, 6, 8-11, 17, 18, 45-49, 51 and 54-56 are anticipated by Satyamoorthy.

24. Claims 1, 2, 6, 8-10, 12, 15-18, 32, 45-47, 51, 53-55, 57, 60 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Cotten et al., 1992 (PNAS, USA, Vol. 89, pp. 6094-6098).

The claims are directed to a vector for delivery of a virus, such as a retrovirus or an adenovirus, to a target cell within a host animal, comprising a cell targeting ligand, such as a protein, a peptide or a hormone, non-covelently bound directly to said virus, wherein said virus and said ligand are not naturally associated with each other, a method of preparing said vector, and a vector produced by said method. Claims 15 and 16 specify the cell-targeting ligand and the virus are present at a ratio in the range of 1ug to 10mg and 10ug to 600ug of said ligand per 10^{10} virions, respectively. Claims 10 and 55 specify the cell-targeting ligand is a native protein or a recombinant protein. Claims 12 and 57 specify the cell-targeting ligand is transferrin. Claims 60 and 61 specify the cell-targeting ligand and the virus are present at a ratio in the range of 1ug to 10mg and 10ug to 600ug of said ligand per 10^{10} virions, respectively.

Cotten teaches mixing a plasmid DNA expressing luciferase under the control of RSV promoter with human or mouse transferrin-polylysine (equivalent to 4ug of polylysine) and the mixed solution is further mixed with a replication-defective human adenovirus 5 lacking functional E1a sequence (e.g. p. 6095, left column, 3rd paragraph, right column, 3rd paragraph). Cotten further teaches mixing the mouse transferrin-polylysine (mTfpL) with 10 ul of adenovirus

dI312 containing $5x10^{11}$ particles/ml (e.g. Figure 3). The virus particle is functioning in trans and the DNA to be delivered is not incorporated within the virus capsid (e.g. p. 6094, right column, 2nd paragraph). The transferrin is the cell-targeting ligand and the replication – defective adenovirus is considered a recombinant virus. The transferrin is not covalently bound to the adenovirus. Ten ul of adenovirus dI312 containing $5x10^{11}$ particles/ml equals to about $5x10^{9}$ adenovirus particles. Therefore, the ratio of ligand and virus is within the range of 1ug to 10mg or 10ug to 600ug of ligand per 10^{10} virions. Thus, claims 1, 2, 6, 8-10, 12, 15-18, 32, 45-47, 51, 53-55, 57, 60 and 61 are anticipated by Cotten.

25. Claims 1, 2, 6, 9-11, 15-18, 32, 45-47, 51, 54-56, 60 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Seth et al., 1984 (Journal of Virology, Vol. 51, No. 3, p. 650-655).

The claims are directed to a vector for delivery of a virus, such as a retrovirus or an adenovirus, to a target cell within a host animal, comprising a cell targeting ligand, such as a protein, a peptide or a hormone, non-covelently bound directly to said virus, wherein said virus and said ligand are not naturally associated with each other, a method of preparing said vector, and a vector produced by said method. Claims 15 and 16 specify the cell-targeting ligand and the virus are present at a ratio in the range of 1ug to 10mg and 10ug to 600ug of said ligand per 10^{10} virions, respectively. Claims 10 and 55 specify the cell-targeting ligand is a native protein or a recombinant protein. Claims 11 and 56 specify the cell-targeting ligand is selected from the group consisting of EGF, VEGF, FGF, IGF, a viral protein and a bacterial protein etc. Claims 60

and 61 specify the cell-targeting ligand and the virus are present at a ratio in the range of 1ug to 10mg and 10ug to 600ug of said ligand per 10^{10} virions, respectively.

Seth teaches preparation of recombinant PE-EGF (Pseudomonas exotoxin and epidermal growth factor) hybrid toxin and mixing adenovirus and PE-EGF in 1.5 ml of fresh medium. The concentration of adenovirus is 0.1 to 10ug/ml and the concentration of PE-EGF is 0.01 to 0.5ug/ml. The mixture was added to KB cells, which was planted at $5x10^5$ cells per 35 mm dish to 80-90% confluency. A suspension of adenovirus at a concentration of 0.1ug/ml contained, one the average, $9x10^2$ particles/cell (e.g. p. 650, right column). Seth teaches that a conjugate of PE-EGF inhibits protein synthesis in KB cells, and the inhibition is increased by adenovirus (e.g. abstract). There are about at least $4.5x10^8$ adenovirus particles per 35mm dish ($9x10^2$ particles/cell multiplied by $5x10^5$ cells), in which 1.5 ml of PE-EGF at a concentration of 0.01 to 0.5ug/ml is used. Therefore, the ratio of the cell-targeting ligand and adenovirus is within the range of 1ug to 10mg and 10ug to 600ug of said ligand per 10^{10} virions. EGF is a cell-targeting ligand and the PE-EGF hybrid toxin is not covalently bound to the adenovirus. Thus, claims 1, 2, 6, 9-11, 15-18, 32, 45-47, 51, 54-56, 60 and 61 are anticipated by Seth.

26. Claims 1-12, 17, 18, 32, 34 and 45-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Spooner et al., 1994 (WO 94/10323).

The claims are directed to a vector for delivery of a virus, such as a retrovirus or an adenovirus, to a target cell within a host animal, comprising a cell targeting ligand, such as a protein, a peptide or a hormone, non-covelently bound directly to said virus, wherein said virus and said ligand are not naturally associated with each other, or said virus comprises a therapeutic

nucleic acid encoding a therapeutic protein, such as p53, a method of preparing said vector, and a vector produced by said method. Claims 7 and 52 specify the virus is selected from the groups consisting of AAV, herpes simplex virus, cytomegalovirus, vaccinia virus, fowlpox virus, canarypox virus and Sandbis virus. Claims 8 and 53 specify the virus is a chimeric virus, a hybrid virus or a recombinant virus. Claims 10 and 55 specify the cell-targeting ligand is a native protein or a recombinant protein. Claims 11 and 56 specify the cell-targeting ligand is selected from the group consisting of EGF, VEGF, FGF, IGF, a viral protein and a bacterial protein etc. Claims 12 and 57 specify the cell-targeting ligand is transferrin.

Spooner teaches preparation of a virus or virus-like particle, such as vaccinia virus, adenovirus, any other animal virus or replication-defective derivative thereof, having a modified binding specificity conferred by a binding moiety, such as a ligand of a target cell-specific cell-surface receptor, allowing the virus or virus-like particle to bind to a target cell (e.g. p. 77). The binding moiety could be EGF or transferrin (e.g. p. 10). The virus or virus-like particle is modified further to contain a gene suitable for gene therapy, such as cytosine deaminase and thymidine kinase (e.g. p. 17, 79) or tumor suppressor gene, for example p53 (e.g. p. 20). Spooner further teaches that the binding moieties which are polypeptides can be synthesized independently of the virus or virus-like particle by expression from a suitable vector in a suitable host and then joined to the virus or virus-like particle (e.g. p. 13, fifth paragraph). The binding moiety polypeptide may be linked to the polypeptide on the surface of the virus or virus-like particle by any of the conventional ways of cross-linking polypeptides (e.g. p., 23, first paragraph). Therefore, the binding moiety (ligand) can be non-covalently bound to the virus or virus-like particle. Thus, claims 1-12, 17, 18, 32, 34 and 45-57 are anticipated by Spooner.

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claims 1, 13, 14, 46, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Cotten et al., 1992 (PNAS, USA, Vol. 89, pp. 6094-6098) or Seth et al., 1984 (Journal of Virology, Vol. 51, No. 3, p. 650-655).

The claims are directed to a vector for delivery of a virus to a target cell within a host animal, comprising a cell targeting ligand non-covelently bound directly to said virus, wherein said ligand binds directly to a receptor on said target cell. Claims 13 and 14 specify the cell-targeting ligand and the virus are present at a ratio in the range of 100 to 1,000,000 and 6,700 to 4,000,000 ligand molecules per virion, respectively. Claims 58 and 59 specify the cell-targeting ligand and the virus are present at a ratio in the range of 100 to 1,000,000 and 6,700 to 4,000,000 ligand molecules per virion, respectively.

The teachings of Cotten and Seth are as discussed above. Cotton or Seth does not specifically teach the ratio of the cell-targeting ligand and the virus in the range of 100 to 1,000,000 or 6,700 to 4,000,000 ligand molecules per virion.

It would have been obvious for one of ordinary skill in the art at the time of the invention to use the ratio of the cell-targeting ligand and the virus in the range of 100 to 1,000,000 or 6,700 to 4,000,000 ligand molecules per virion because Cotton teaches mixing the mouse transferrin-polylysine (mTfpL) with 10 ul of adenovirus dI312 containing $5x10^{11}$ particles/ml, and Seth teaches mixing adenovirus and PE-EGF in 1.5 ml of fresh medium and the concentration of adenovirus is 0.1 to 10ug/ml and the concentration of PE-EGF is 0.01 to 0.5ug/ml. Although Cotton and Seth do not specifically teach the range of 100 to 1,000,000 or 6,700 to 4,000,000 ligand molecules per virion, however, the concentrations of the adenovirus and ligand taught by either Cotten or Seth might have already fallen with the range claimed. Even if the concentrations of the adenovirus and ligand taught by either Cotten or Seth do not fall with the claimed range, it would be obvious for one of ordinary skill in the art at the time the invention was made to use the claimed range of ration of the adenovirus and ligand in order to provide better protein synthesis in KB cells by PE-EGF as taught by Seth or to provide high-efficiency receptor-mediated gene delivery via the use of defective adenovirus particles as taught by Cotton with reasonable expectation of success.

30. Claims 1 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spooner et al., 1994 (WO 94/10323) in view of Kingsman et al., 1997 (WO 97/32026).

The claims are directed to a vector for delivery of a virus to a target cell within a host animal, comprising a cell targeting ligand non-covelently bound directly to said virus, wherein said ligand binds directly to a receptor on said target cell. Claim 36 specifies the virus is retrovirus or herpes simplex virus comprising a therapeutic nucleic acid and said ligand is transferring.

The teaching of Spooner is as discussed above. Spooner does not teach using retrovirus having a transferrin as a ligand for gene delivery to target cells.

Kingsman teaches a retroviral particle having molecular adapter molecules for gene therapy and for targeting retroviral delivery vector to specific target cells. The adapter molecule comprises a first amino acid sequence, such as EGF, having binding affinity for a cell surface molecule and a second amino acid sequence having binding affinity for a viral surface molecule (e.g. abstract, p. 1). The first and second amino acid sequences are linked in the adapter molecule either covalently or non-covalently. The non-covalent linking includes streptavidin-biotin bridges and other binding partners (e.g. p. 4, 2nd paragraph).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use retrovirus having a transferrin as a ligand for gene delivery to target cells because Spooner teaches using adenovirus or vaccinia virus having a transferrin as a ligand for gene delivery in gene therapy and Kingsman teaches using retrovirus for gene delivery in gene therapy.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to deliver gene to target cells in gene therapy as taught by Spooner and Kingsman with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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PRIMARY EXAMINER